



Original Research Article

Comparasion of intravenous Nalbuphine versus intravenous Paracetamol for postoperative analgesia in patients undergoing surgeries under general anaesthesia

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ARTICLE INFO

Article history:

Received 25-07-2019

Accepted 16-10-2019

Available online 20-11-2019

Keywords:

Intravenous Nalbuphine
Paracetamol
postoperative analgesia
VAS score
Haemodynamic variables
sedation

ABSTRACT

Introduction: Postoperative pain is the most annoying symptom that every patient will complain after the surgery. Relief of this pain greatly improves the patient satisfaction, compliance and recovery. Opioids and NSAIDs are the most commonly used analgesics in the postoperative period. The need for the study was to compare the efficacy of intravenous Nalbuphine over intravenous Paracetamol in the postoperative period.

Materials and Methods: 60 patients who underwent elective surgeries under general anaesthesia were selected for the study. 30 patients in Group P received Inj. Paracetamol 15 mg/kg body wt. and 30 patients in Group N received Inj. Nalbuphine-0.15 mg/kg body wt over 15 min. Both the groups received the study drug half an hour before the completion of surgery.

Postoperative pain scores were measured using VAS pain score and postoperative haemodynamic parameters were measured at regular intervals. The time for the first dose of rescue analgesia was noted. Side effects like sedation, nausea, vomiting, pruritus were assessed at regular intervals postoperatively until 10 hours.

Results: Demographic profile were comparable between the groups. Both Nalbuphine and Paracetamol can be effectively used for treating postoperative pain. But Nalbuphine is used as safer alternative since the duration of analgesia is longer in Nalbuphine group when compared to Paracetamol group without significant side effects. Haemodynamic stability was maintained in both the groups.

Conclusions: IV Nalbuphine is a better cost effective alternative to IV Paracetamol in alleviating the postoperative pain with prolonged duration of analgesia and hemodynamic stability without significant side effects.

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1. Introduction

Pain is one of the most common reasons for seeking medical assistance.¹ The International Association for the Study of Pain (IASP) has defined pain as “It is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.²

Postoperative pain is of acute type and very much distressing to the patient although it has a protective function and protects the injured body part while it heals.³ Postoperative pain relief is a major concern and many analgesics have been used in this regard. Morphine is the standard opioid analgesic used for this purpose.⁴ However

due to its intolerable side effects like nausea, vomiting, pruritus etc, many other drugs have been tried. One of the drugs is Nalbuphine. Nalbuphine is a newer opioid synthesized, that has both opioid agonist and antagonist properties. It does not have the deleterious side effects of morphine and has been successfully used for the postoperative pain relief.⁴

On the other hand, intravenous (IV) Paracetamol has also been successfully used for postoperative pain relief without any side effects of opioids.

In our study we are comparing the efficacy of intravenous Nalbuphine and intravenous Paracetamol for postoperative analgesia in patients undergoing elective surgeries under general anaesthesia.

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2. Materials and Methods

This is a randomized double blind study conducted at Hassan Institute of Medical Sciences over a period of one year. Randomization was done using a computer generated numbers in which patients were randomly allocated into two groups-Group P and Group N. Each group consisted of 30 patients and they were selected after fulfilling the inclusion and exclusion criteria.

2.1. Inclusion criteria

Patients aged between 20 and 60 years of age of both the genders and who were posted for elective surgeries under general anaesthesia of ASA I and II status were included in the study.

2.2. Exclusion criteria

Age < 20 years and >60 years, patients with history of allergy to either Nalbuphine or Paracetamol, uncontrolled diabetic and hypertensive patients, patients with history of coagulopathies, pregnant ladies and lactating mothers, history of coronary artery disease and congenital heart disease, patients on any other sedatives on regular basis like antipsychotics, antiepileptic drugs, were excluded from the study.

On the day before the scheduled surgery, a thorough preanesthetic evaluation was done for all the patients. During their preanaesthetic visit, patients were explained about the study procedure and about VAS scoring that will be used in the postoperative period.

On the day of surgery, in the preoperative room, an intravenous cannula was placed on the dorsum of the left hand and crystalloid infusion started. Patients were then shifted to operation room. In the operation room, minimum mandatory monitoring was carried out. A multiparameter monitor was used for this purpose. Continuous monitoring of heart rate, blood pressure, peripheral oxygen saturation (SpO₂) and electrocardiogram was carried out throughout the procedure.

General anaesthesia was administered for all patients. Premedication was done with Inj. glycopyrolate-0.2mg, Inj-Ondansetron-4mg, Inj. Ranitidine-50mg, Inj, midazolam-0.5mg, and Inj.fentanyl-50microgm. Induction of anaesthesia was done with Inj. Thiopentone-5mg/kg. body wt.. After the loss of eyelash reflex and confirming the adequacy of mask ventilation, Inj, succinylcholine-2mg/kg. body wt. was administered. After waiting for 60 seconds, intubation was attempted with Macintosh laryngoscope and proper size cuffed endotracheal tube was inserted. Maintenance of anaesthesia was done with mixture of nitrous oxide and oxygen(66%:33%) along with isoflurane (0.5-1%) along with the top up doses of vecuronium.

Half an hour before the completion of procedure, study solution was given in both the groups for a period of 15

minutes. The study solution was prepared by a person who was not a part of the ongoing study. Both the study drugs were diluted to 100 ml of normal saline before administration.

As there were 60 patients in our study, two groups (Group P and Group N) were made with 30 patients in each group. Group P patients were administered Inj. Paracetamol 15 mg/kg body wt. and patients in Group N were administered Inj. Nalbuphine-0.15 mg/kg body wt.

At the end of the procedure, patients were administered Inj. neostigmine (0.05 mg/kg body wt.) and Inj. glycopyrrolate (0.01 mg/kg body wt.) to reverse the effects of muscle relaxants and patients were extubated. Immediately after extubation (0hr), VAS score and haemodynamic parameters were recorded. The patients were then transferred to the postoperative recovery room and all the parameters required for our study were recorded by the blinded investigator.

In postoperative recovery room, patients were enquired about the pain and was recorded using Visual Analogue Scale which was explained to them during their preanaesthetic visit. VAS score was recorded at regular intervals and the patients were given rescue analgesia with Inj. Diclofenac 75 mg intramuscularly when VAS score reached >3. The time for the first dose of rescue analgesia was recorded in both the groups.

Haemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at regular intervals of 30 min, 1 h, 2 h, 4 h, 6 h, 8 h and 10h. Sedation level was assessed using Pasero Opioid-induced Sedation scale.

Most common side effects of opioids like nausea, vomiting, respiratory depression and pruritus were also noted.

The postoperative sedation level was assessed by 4-point Pasero Opioid-induced Sedation Scale⁵ which is as follows

1- awake and alert; 2-slightly drowsy, easily aroused; 3-frequently drowsy, arousable, drifts off to sleep during conversation; and 4- somnolent, minimal or no response to verbal or physical stimulation

2.3. Statistical analysis

We have used SPSS 16.0 software for analyzing the data of our study. Descriptive statistics was used to study the demographic profile of the patients. Non Parametric test like Chi-square test was used to test the significance between two groups with regard to time for rescue analgesia. Parametric test like Mann – Whitney *U* test was used to find the difference in the median scores. *P* value < 0.05 was considered as statistically significant.

3. Results

We carried out the study in 60 patients who were divided into 2 groups of 30 each and we used either Inj. Nalbuphine 0.15 mg/kg body wt. or Inj. Paracetamol 15 mg/kg body wt. for treating the postoperative pain.

Both groups were comparable with respect to demographic profile which is shown in (Table 1).

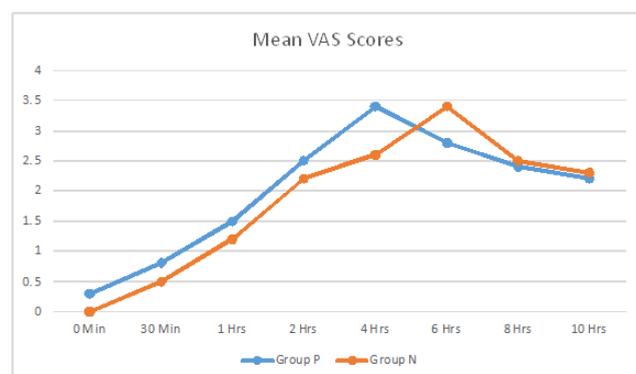
Comparison of VAS scores is shown in the Graph 1. VAS scores were comparable in between two groups immediately after surgery, at 30 min., 1 hrs., and 2 hrs. But VAS showed a significant difference at about 4 hrs with Mean VAS score of 3.5 in group P, whereas in group N, mean VAS score of 3.4 was observed at about 6 hrs. (Graph 1)

Haemodynamic parameters observed in the study are shown in the (Graphs 2 and 3). There was no statistically significant difference between two groups in the haemodynamic parameters like mean heart rate and mean arterial blood pressure and respiratory rate ($p > 0.05$).

Time for the first dose of rescue analgesia (Duration of analgesia) was significantly longer in group N (6.25 ± 1.06 hours) compared to group P (4.25 ± 0.76 hours) with P value < 0.005 which is shown in (Graph 4)

Incidence of postoperative nausea, vomiting, pruritus and respiratory depression were comparable in both the groups as cited in (Graph 5)

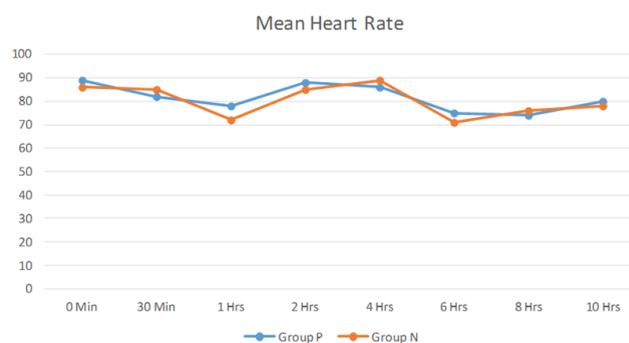
Postoperative sedation scoring was done with 4-point Pasero Opioid-induced Sedation Scale. The median sedation scores immediately after surgery (0hr) and 30 min. after the surgery in Group P was 1, whereas in Group N, it was 2, which was significant; ($P < 0.05$). However after 1 hrs, median sedation scores were comparable in both the groups ($P > 0.05$) at all intervals.



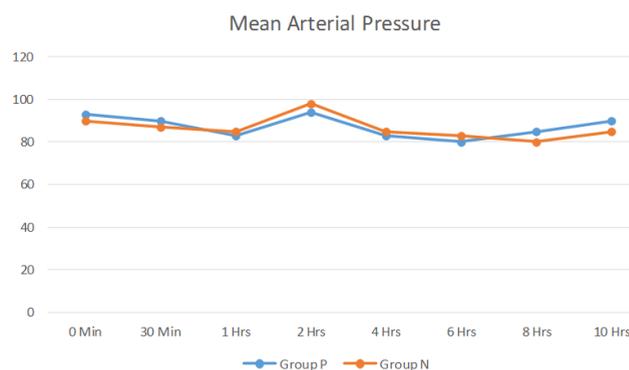
Graph 1: Comparison of mean VAS scores between the two groups

4. Discussion

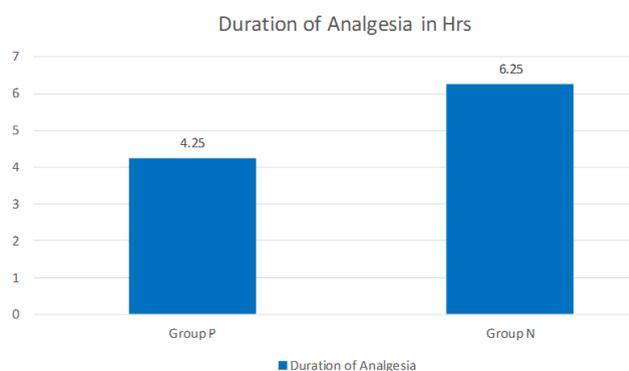
Postoperative pain management is a key to good surgical outcome. From ages, Opioids and NSAIDs have been used in various routes to combat postoperative pain.



Graph 2: Comparison of mean Heart rate between the two groups at various intervals



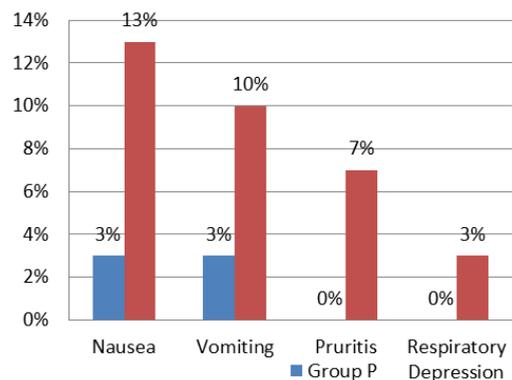
Graph 3: Comparison of mean arterial pressure between the two groups at various intervals



Graph 4: Comparison of duration of analgesia between the two groups

Table 1: Distribution of Patients based on Age, Body weight, Gender Ratio, Duration of surgery and ASA status

	Group- P(n=30)	Group-N(n=30)	P- Value
Mean Age \pm SD (Yrs)	39.3 \pm 8.13	42.2 \pm 7.12	0.652
Mean Body Weight \pm SD (Kgs)	55.12 \pm 8.24	54.18 \pm 7.86	0.452
Gender Ratio (M:F)	20:10	22:8	0.563
Duration of surgery: (Mins)	140.72 \pm 8.13	130 \pm 7.12	0.456
ASA I/II	25/5	23/7	0.502



Graph 5: Comparison of side effects between the two groups.

Most common opioid analgesic used to treat varieties of pain is Morphine. Morphine has been used in various routes and different dosages to treat a wide range of pain including cancer pain. But when it is used on regular basis, many patients will complain of intolerable side effects like nausea, vomiting, pruritus etc. Hence they change over to other drugs.⁴

In an attempt to provide analgesia without the unwanted side effects of the pure agonists, Nalbuphine was synthesized.⁶ Nalbuphine has both agonist and antagonist properties on opioid receptors. It acts on both μ and κ -receptors that results in its analgesic and anti-pruritic effects. It also exhibits ceiling effect for respiratory depression.⁷ It is commonly used nowadays for treating postoperative pain.

Paracetamol (acetaminophen) is most commonly used as an antipyretic agent for the treatment of fever in adults and children. Previously oral route of administration was commonly used for paracetamol. But in 2010, it was reintroduced in IV form. As it does not belong to NSAID group of drugs, it is devoid of the side effects of NSAIDs.⁸ Hence, it has become a safer alternative to NSAIDs for treating different types of pain.

Studies⁸⁻¹² has shown the analgesic effects of paracetamol in both adults and children during surgeries. It is also been compared with many other drugs like NSAIDs,⁹ Opioids^{8,10,11} and Gabapentin.¹²

Mohammed shahid et al,⁸ has done a study to compare paracetamol and tramadol administered intravenously in

alleviating the pain in the postoperative period. Patients received Inj. paracetamol 1g or Inj. tramadol 2 mg/kg slow IV 30 min before the end of the procedure. Results from their study showed that paracetamol given intravenously is a better and safer alternative when compared to tramadol for the treatment of postoperative pain. Side effects like nausea and vomiting are lower in paracetamol group than in tramadol group. This resulted in decreased duration of hospital stay and earlier discharge of the patient.

In a study done by Kumkum et al,⁹ intravenous paracetamol (1gm) was compared with intravenous parecoxib (40mg). The study drug was administered over a period of 15 minutes after 30 minutes of induction. They have concluded that Inj. parecoxib was compared favourably with Inj. paracetamol. Patients well tolerated both the study drugs. There was no derangements in the haemodynamic parameters in both the groups, Added advantage of parecoxib was its of longer duration of action when compared to paracetamol.

Uysal et al¹⁰ has compared IV paracetamol and IV tramadol for their analgesic properties in postadenotonsillectomy pediatric patients. Patients in paracetamol group were given 15 mg/kg of paracetamol and the patients in tramadol group were given 1.0 mg/kg of intravenously. They concluded that both IV paracetamol and IV tramadol have similar analgesic properties but IV paracetamol is associated with early recovery when compared to IV tramadol after adenotonsillectomy in children.

Pendeville et al¹¹ have done a study in children undergoing day care tonsillectomies to compare paracetamol and tramadol for postoperative pain relief. They gave IV paracetamol 30 mg/kg or tramadol 3 mg/kg before surgical incision. For postoperative analgesia, each child received either tramadol drops 2.5 mg/kg or paracetamol suppositories 15 mg/kg. They concluded that children who were given tramadol have lower pain scores in postoperative period. Use of rescue analgesics was also significantly lower in the tramadol group.

Similar to the study done by Pendeville et al,¹¹ Sabry M Amin et al¹² has compared gabapentin and paracetamol as premedication in the treatment of postoperative pain in children undergoing adenotonsillectomy. They gave gabapentin 10 mg/kg and paracetamol 20 mg/kg through oral route, two hours before the induction of anaesthesia. Results from their study showed that oral gabapentin given as premedication has better postoperative analgesia when

compared to oral paracetamol. It also reduces analgesic requirements in comparison with paracetamol. These two studies show that tramadol and gabapentin are better analgesics than paracetamol for postoperative pain.

Many studies have been done to know the efficacy of nalbuphine in the field of anaesthesia especially in intraoperative and postoperative period.

R N Solanki et al¹³ has done a comparative study between intravenous nalbuphine and intravenous tramadol in patients undergoing surgeries under regional or general anaesthesia. IV Nalbuphine 0.15 mg/kg and IV tramadol 2 mg/kg was used 8th hourly. VAS scores, sedation score and total number of rescue analgesics were noted at regular intervals. They concluded that Nalbuphine is better analgesic for the relief of moderate to severe postoperative pain and also provides good sedation, hemodynamic stability and lower incidence of nausea & vomiting. The study results are similar to our study compared to tramadol. Dosage of nalbuphine used in our study is similar to the above study.

In a similar study done by Jitesh kumar et al.¹⁴ Inj, nalbuphine 0.25 mg/Kg and inj. tramadol 2 mg/kg have been compared in short surgical procedures. Both drugs were given 5 minutes before induction and postoperative VAS score, haemodynamic parameters, sedation scoring were noted. They have also come to the conclusion that nalbuphine is a better analgesic than tramadol for short surgical procedures, and it provides a better relief of postoperative pain with good sedation, hemodynamic stability and lower incidence of PONV.

The results from the above two studies are similar to our study.

Nalbuphine has also been compared with fentanyl¹⁵ and pentazocine¹⁶ to study its effects on the intubation response and analgesic requirements intraoperative and postoperatively. Results from these studies showed a favourable outcome towards nalbuphine and they have concluded that it can be used for attenuation of pressor response of tracheal intubation and for perioperative analgesia with minimal side effects.

In our study we have compared IV paracetamol with IV nalbuphine for the treatment of postoperative pain in patients who are posted for elective surgeries under general anaesthesia, which is first of its kind till now. This type of study is not conducted so far. Hence, we decided to carry on with the study. In Group P, mean VAS scores showed a sharp rise (>3) after mean duration of 4.25±0.76 hours. The rescue analgesia in the form of Inj. Diclofenac was given after approximately 4 hours in Group P. In Group N mean VAS scores showed a rise (>3) after 6.25±1.06 hours. The rescue analgesia was given after approximately 6 hours in Group N. By this, we came to conclusion that duration of analgesia with nalbuphine is longer than paracetamol.

5. Conclusion

In this modern era of anaesthesiology, a very good postoperative pain relief is a key to the earlier recovery. Good postoperative analgesia results in better surgical outcome, lessens the duration of hospitalization and hence early discharge of the patient. As seen from the results of our study, both IV paracetamol and IV nalbuphine can be effectively used to treat postoperative pain although IV nalbuphine is a better cost effective alternative to IV paracetamol in alleviating the postoperative pain with prolonged duration of analgesia and good hemodynamic profile without significant side effects. Unlike other opioids, the availability of nalbuphine is made easy since it does not require narcotic licence.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Rashmi H D , Airani HV. Comparison of intravenous Nalbuphine versus intravenous Paracetamol for postoperative analgesia in patients undergoing surgeries under general anaesthesia. *Indian J Clin Anaesth* 2019;6(4):553-558.

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